NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND (NMRDC)

I. Background.

Commissioned in 1974 as an Echelon III headquarters activity, NMRDC is located on the grounds of the Naval Medical Command, National Capital Region in Bethesda, Maryland as a Tenant Command. Its new offices are located on the tenth through twelfth floors of the old hospital tower (Building 1). The Command was derived from the office of the former Director of Research at the Bureau of Medicine and Surgery (Codes 7 & 71).

NMRDC has the responsibility for the management support, review, and oversight of a worldwide laboratory network conducting a diverse program of Navy medical research and development in:

- o Combat Casualty Care with emphasis on the needs of the Fleet Marine Force, particularly in extreme environments.
- o Physiological and psychological aspects of health and the effective performance of Navy and Marine Corps personnel.
- o Submarine and Diving Medicine as related to decompression safety, and effective performance of Navy personnel.
- o Aviation Medicine related to safety and the effective performance of Navy and Marine Corps personnel.
- o Dental diseases and emergencies with emphasis on prevention and management of cases in operational environments.
- o Human effects of mechanical forces including motion, impact and vibration encountered on ships and aircraft.
- o Infectious diseases of military importance encountered by Navy and Marine Corps personnel in the conduct of Fleet operations worldwide.
- o Maintaining the science and technology base necessary to respond to fleet and medical requirements as they arise in the unique operating environments imposed by Fleet operations.

II. Laboratories.

To accomplish this mission, NMRDC has eight commissioned Echelon IV laboratories, and three commissioned Echelon V detachments of

two laboratories, geographically dispersed to take advantage of the environment, unique Navy and Marine Corps populations, and unique capabilities located in specific areas.

A. **Continental United States.**

Naval Aerospace Medical Research Laboratory	Pensacola, FL
Naval Biodynamics Laboratory	New Orleans, LA
Naval Dental Research Institute	Great Lakes, IL
Naval Health Research Center	San Diego, CA
Naval Medical Research Institute	Bethesda, MD
NMRI Toxicology Detachment- WPAFB	Dayton, OH
Naval Submarine Medical Research Laboratory	Groton, CT

B. **Overseas Laboratories.**

Naval Medical Research Unit No. 2 (NAMRU-2)	Manila, RP
NAMRU-2 Detachment	Jakarta, ID
Naval Medical Research Unit No. 3 (NAMRU-3)	Cairo, A.R.E.
NMRI Detachment (NAMRID)	Lima, PE

All laboratories are made up of a mixed military and civilian staff, bringing a cadre of dedicated professional, technical, and support personnel to bear on the problems encountered by U. S. Navy and Fleet Marine Force personnel in the conduct of normal peacetime operations and potential problems associated with disease and injury resulting from armed conflicts. Our current staffing includes:

Military Officers	204
Military Enlisted	317
Civilian Professional*	212
Civilian Technical and Support	184
Foreign National	312
	1229

The skill mix includes a wide diversity from 54 occupational specialties* in medicine and the allied health sciences including physicians, dentists, physiologists, optometrists, psychologists, biochemists, microbiologists, immunologists, engineers, physicists, computer specialists, mathematicians, etc. This is not unusual considering that the range of scientific responsibility covers a spectrum as depicted in the following

*Using the criterion established by the Office of Personnel Management.

diagram:

Normal Man — Abnormal Man

Dysfunction — Disorder — Disease/Injury

Abnormal — Environment — Normal

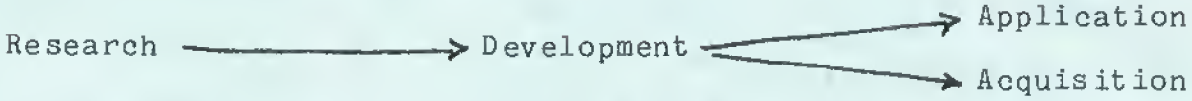
III. **Scientific Program Structure.**

The Navy Medical Research and Development Program derives from several sponsors who expand on a source document called Defense Guidance. Sponsorship for R&D programs results from policies established by Public Law and responsibilities passed to the highest levels of DOD, SECNAV, and OPNAV. Therefore, through the Naval Medical Command, NMRDC is responsible for scientific program execution, program justification, and resource utilization, to multiple sponsors who each have different missions.

Program sponsorship in research, development, test, and evaluation (RDT&E) deals with the congressional appropriations and authorizations associated with Defense Appropriation Program Six, RDT&E. NMRDC is Navy Medicine's only organization supported by the Program Six appropriation. The RDT&E program is broken down as listed in the following table:

Program Element	Description	Sponsor
6.1	Research	ONR
6.2	Exploratory Development	ONT
6.3	Advanced Development	OP-02, 05, 093
6.4	Engineering Development	OP-093
6.5	Management & Support	OP-02,OP-098
Medical Chemical Defense	US Army (6.1- 6.3)	USA SG
Medical BW Defense	"	(USAMRDC)
Combat Dentistry	"	"
Infectious Disease	"	"
Other Reimbursible Work	"	OP-31, SYSCOMS, USPHS, NASA, etc.

This RDT&E program is based upon an industrial model designed to result in tangible products.



The easiest way to look at Navy Medicine's research and development program is to reorganize related science and technology, irrespective of funding categories into research areas called "thrusts". NMRDC's research program thrusts are in the following areas:

- Combat Casualty Care
- Submarine and Diving Medicine
- Performance Assessment and Enhancement/Aviation Medicine
- Infectious Disease
- Environmental Medicine and Occupational Health
- Dentistry

All of the components have Program Element 6.1 through 6.3 funding. Currently, all of our 6.4 engineering development resources are dedicated to one product under development - the Resuscitation Fluids Production System (REFLUPS). All of our work is done by in-house laboratories and extramural contracts (with other agencies, universities, and industry).

In recent years an adjustment in the focus of our medical research and development programs has occurred. More and more scientific work is conducted in the field; onboard ships, deployed during exercises, mobile laboratories deployed to operational sites. This is in addition to our very sophisticated, well-equipped in-house facilities. The thrust of this approach involving all of our programs is to acquire relevance by learning how to scientifically cope with the "criterion environment". Navy and Marine Corps operations do not occur in the laboratory, but in the real world. To successfully study the problems encountered in the multiple operational environments into which the Fleet and the Fleet Marine Force deploy, we have to scientifically define what is happening in the real world so we can produce a valid laboratory condition to isolate and deal with the problems. Too often in the past, the laboratory result would not generalize to the field situation because more attention was paid to the biological phenomenon than to the setting in which it was found. In short, what we do in research has not changed, but why and how we do it in context has changed dramatically. In the process, Medical R&D has found a way to be more rapidly responsive to Fleet requirements. In the

process of studying medical and biological events in the real world, we can deliver recommendations for various actions by the Fleet commanders or medical support staff that have immediate benefit. This "buys time" by providing for a more effective fighting force while we wrestle more conventionally and scientifically with mother nature to extract her secrets.

IV. Conduct of Research and Development in the Field.

In 1986-88 components of NMRDC have participated in the following exercises and deployments:

1. UNITAS/WATCC traveling with embarked units around Central and South America over to Africa.

2. BRIGHT STAR deployed to Egypt.

3. COBRA GOLD exercised in Thailand and the Pacific Rim.

4. Deployed research teams in 15 countries around the world on five continents.

a. AIDS incidence and prevalence in Africa, Asia and South America to describe the potential risk to deployed U.S. Forces.

b. Conduct prophylaxis and therapeutic trials for hepatitis, typhoid, malaria, rickettsial diseases.

c. Conducted studies in tropical infectious disease epidemics involving in dengue fever, leishmaniasis, chikungunya fever, Korean hemmorhagic fever, Japanese encephalitis and hepatitis.

d. Studied the combination of heat stress, chronic fatigue, and performance degradation under continuous potential battle conditions in the Persian Gulf.

5. Operated mobile laboratories in Navy operational shore activities studying vision, fitness, psychological and physiological performance in aviation personnel, ground support personnel, and sonar operators.

6. Performed site visits in areas where cold weather training will be conducted in the future to plan mobile field laboratory studies.

7. Completed a preliminary study in the Antartic on endocrine metabolic, and performance effects in the extreme cold.

8. Sent a team to Puno, Peru in the Andes to diagnose, evaluate, and treat a fever of unknown origin that resulted in significant morbidity and mortality among the indigenous population.

9. Sent an investigative team to Clark AFB in the Philippines to diagnose and assist in the treatment of a Japanese encephalitis outbreak.

V. Accomplishments and Progress: Fundamental Research

A. Wound treatment technologies to promote hemostasis, speed healing, prevent infection, and reduce scarring.

1. Stimulate collagen cross-linking.

2. Liquid collagen dressings.

3. Antibiotic beads impregnated in wounds to prevent sepsis.

4. Chitosan impregnated field dressings to provide for immediate cessation of capillary bleeding in the field.

B. Surgical support research.

1. Sutureless anastomosis of severed blood vessels using annealing rings sensitive to heat.

2. Wound lavage using hypertonic glucose to break the microscopic mechanical bonds of bacteria to tissue.

3. Covalent linkages stimulated by endothelial growth factors to promote restoration of the lining of natural or prosthetic blood vessels and prevent blood clotting.

4. Use of growth factors to promote angiogenesis and bone growth so bone grafting techniques can be more effectively used.

5. Developing methods to reverse problems created by small blood vessel refractoriness during injury that contribute to shock.

C. Immunobiology research

1. Isolated and produced hematopoietic stem cells in sufficient quantities to be able to conduct experiments in

controlling differentiation of stem cells into useful types. We have completed successful marrow regeneration in vivo from a stem cell population.

2. Begun using stem cells and growth factors to produce immune cell proliferation in desired directions, such as making leukocytes (white blood cells). These technologies can be used ultimately to restore immune systems damaged by disease, burns, or injury.

3. Exploitation of control over cellular immunity in the development of vaccines and the human response to toxic events (infection, chemical exposure, etc.).

D. Blood and blood products.

1. The use of liposome encapsulated hemoglobin as a blood substitute.

2. Enzymatically converting the components of Type A and Rh positive blood cells making them Type O, Rh negative.

3. Commenced clinical trials of red blood cells that have been enzymatically converted to Type O from Type B.

E. Developed and used monoclonal antibodies for early diagnosis of dental disease.

VI. Accomplishments and Progress: Applications Oriented Research

- o Achieved licensure of red blood cells frozen in the primary collection bag, stored for ten years at -80 c, and thawed for use.
- o Completed operational demonstration of the liquid frozen blood bank concept aboard the USNS MERCY (T-AH19).
- o Developed a prototype Resuscitation Fluids Production System unit for use in the field and aboard ship.
- o Produced a test unit capable of remotely sensing vital signs in persons or casualties.
- o Develped and achieved licensure for human test of a non-invasive rewarming device to treat exposure and hypothermic casualties, which uses radiofrequency generating induction coils.

- Developed a field useable assay for body fluid levels of bacterial toxin (lipopolysacchiaride) as an indicator of the presence of septic shock.

- Developed a field pourable collagen-based battle dressing.

- Developed and validated the physical fitness test batteries used in the Navy's health and physical readiness programs.

- Completed and reported a Navy-wide study of shipboard health care delivery by the Independent Duty Corpsman.

- Developed programs to reduce attrition during Naval Special Warfare training in Basic Underwater Demolition School.

- Completed a dental treatment needs survey.

- Developed a ballistic face shield integrated with combat helmets for testing with the Kevlar helmet.

- Demonstrated superior performance is possible in low level (neutral filtered) white light as opposed to red light on submarines and surface vessels with minimal effect on dark adaptation.

- Developed a compact corrective lens periscope insert for use by submariners who require glasses while performing their duties.

- Conducted shipboard tests of a computerized medical diagnosis system for non-physician health care providers.

- Identified the optimum requirements for visual sonar symbol formats and are working to correlate these with optimal auditory cue matches for sonar operators.

- Developed the first statistically validated decompression procedures for air diving using a technique called maximal likelihood analysis.

- Developed and fielded a comprehensive occupational health information management system called NOHIMS to monitor Navy employees engaged in occupations.

- Identified the etiologic agents of diarrheal diseases during the UNITAS/WATCC cruises over the past three years and Operation BRIGHT STAR '87, demonstrating different antibiotic sensitivities by geographic region.

- o Identified and commenced trials for treatment of bacterial diarrhea: Ciprofloxacin in the Middle East and Norfloxacin(s) in South America and the Middle East.

- o Developed the rationale and successfully tested clinically the use of Tensilon (Edrophonium) in the treatment of cobra envenomization in the Philippine archepelago.

- o Developed specific rapid diagnostic tests for use in the field for acute diarrhea and parasitic diseases.

- o Established a clinical research center in Indonesia for the study of the pathophysiology of life threatening tropical disease with emphasis on Dengue and the hemorrhagic fever it produces in its most severe manifestation, dengue shock syndrome. Treated a seaman from the USNS CHAUVENET who became ill on deployment with dengue hemorrhagic fever.

- o Conducted field trials of two candidate oral typhoid vaccines in Plaju, Sumatera, Indonesia.

- o Compared the efficiency of citrate buffer versus bicarbonate buffer oral rehydration in the treatment of the severe secretory diarrhea associated with cholera. Wrote the protocol for the WHO to change its recommendation to the use of citrate buffer solutions.

- o Developed and validated performance-based psychological and physiological tests for medical assessment of applicants to mission specific programs (aviators, submariners, sonar operators, SEALS, etc.). These tests are being used to improve the quality of selection and assignment, reduce attrition, and enhance the effectiveness of people serving our Navy's mission.

- o Assessment of the validity of current medical standards as they pertain to psychological and physiological performance in various warfare specialties, and as they pertain to medical outcomes in the course of a Navy career.

- o Commenced the study of psychological and physiological aspects of performance in cold weather operations (shipboard and amphibious assault) in order to develop methods to protect the individual and improve cold weather performance by behavioral, metabolic, and pharmacological means over sustained periods of time.

- o Developed and tested for fleet introduction protocols

designed to enhance G-tolerance in aviators using a combined fitness program and proper use of straining maneuvers. Program structured to reduce in risk of G-induced loss of consciousness caused by rapid rates of G onset in new tactical aircraft.

The following examples provide some insight into current and future programs worldwide that result in tangible benefits for our forward deployed and permanently stationed personnel around the world. This demonstrates an underlying philosophy of military medical research and development that what we do can and will have direct benefit to the Navy and Marine Corps personnel we are pledged to support. The fact that our work can have tremendous influence on the civilian practice of medicine, and assist developing nations, and provide technology impetus that assists other Federal initiatives (such as the manned space program) are spin-offs that gives more than passing justification and pride in what we do.

Resuscitation Fluid Production System

The ability to manufacture sterile water, free of fever-producing materials (toxins and proteins) and other impurities, for intravenous use literally in the location where the sterile water is required has long been a goal of applied science and engineering. We have been able to make sterile fluids for injection for a long time, or for intravenous use but all of these methods require stocking large inventories of material whose date of expiration usually precede their use. In a military setting this translates to storage space and weight issues that cause most logistics planners to cringe. The financial waste of procurement of large volumes of material that weighs 6.6 pounds per gallon, with a shelf life of three years from the manufacturer, has been considerable. These factors have mildly improved since the placement of these solutions in plastic bags that takes less space than glass bottles. The weight and expiration date problem remains, however.

As a result of our research into the freezing of blood and blood products, we developed a technique of washing the solutions in which blood has been frozen for ten, fifteen, and twenty years. Glycerol, an organic alcohol that formed the basis for the antifreeze industry in automobiles, is the solution in which the blood is frozen. Unfortunately, glycerol is a potent poison that damages kidneys and must be removed from the blood and blood products when they are thawed for use. Removing glycerol and "washing" the blood and cells required a system that could produce its own sterile fluids in large quantities and be used on the thawed blood without damaging the cells. Once produced, it rapidly became apparent that this marriage of several technologies had potential for solving the problem of procurring, storing, and carrying intravenous fluids if it could produce sterile water in sufficient quantities under fleet and Fleet Marine Force operating conditions.

The technology used in producing these fluids involves microfiltration and reverse osmosis working under automated controls. A developmental prototype of the resuscitation fluid production system is currently undergoing testing, and our goal for fleet introduction is in the early 1990's. This device will permit medical units in the field and shipboard Medical Departments to make their intravenous fluids and other sterile fluid requirements on the spot and not be dependent on a logistical supply line for initial use or resupply.